(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 March 2002 (07.03.2002)

PCT

(10) International Publication Number
WO 02/17770 A2

(51) International Patent Classification[7]: A61B

(21) International Application Number: PCT/US01/26593

(22) International Filing Date: 27 August 2001 (27.08.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/227,910 28 August 2000 (28.08.2000) US

(71) Applicants and
(72) Inventors: **MORAND, Patrick, G.** [US/US]; 2529 Kingston Drive, Northbrook, IL 60062 (US). **OSTRO, Marc, J.** [US/US]; 23 West Shore Drive, Pennington, NJ 08534 (US).

(74) Agents: **GARRETT, Arthur, S.** et al.; Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., 1300 I Street, N.W., Washington, DC 20005-3315 (US).

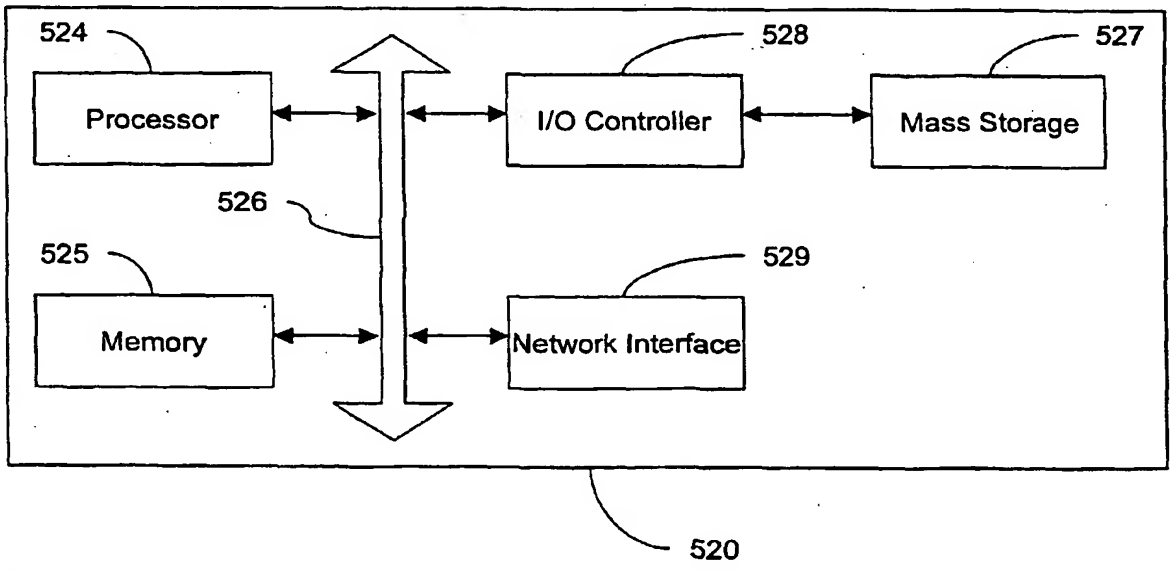
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF BLOOD AND PLASMA DONOR SAMPLES AND DATA IN THE DRUG DISCOVERY PROCESS



(57) Abstract: Systems consistent with the present invention provide a method for identifying and recruiting donors whose demographic characteristics, genomic and proteomic profile, and medical histories make them attractive candidates for clinical trials, drug target identification, and pharmacogenomic studies.

WO 02/17770 A2

USE OF BLOOD AND PLASMA DONOR SAMPLES AND DATA IN THE DRUG DISCOVERY PROCESS

[001] The present invention relates to methods and systems for identifying individuals for clinical trials. More specifically, the present application relates to a method through which the biopharmaceutical industry can gain access to a large and varied population of individuals with a detailed and fully consented medical history as subjects for the clinical trials required for drug development and as sources of research materials. In another aspect, the present invention relates to a method for creating a longitudinal database of biochemical, genomic, and proteomic information as a resource for drug research and development.

[002] Background of the Invention

[003] Clinical and basic research in the biopharmaceutical industry have the objective of discovery, development, governmental approval, and commercialization of therapies and compounds for diagnosing and treating specific diseases. The phases of discovery, development, approval, and marketing are governed by rigorous laboratory, business, and regulatory standards. The efficient recruitment of patients into studies, however, is often referred to as the Achilles Heel of clinical research.

[004] The multi-billion dollar biopharmaceutical industry continues to struggle to attract the interest of both healthy and diseased individuals to participate in clinical and basic research. Entire companies have been organized to recruit volunteers for studies and to collect biological samples to satisfy research needs. Nevertheless, finding the right individuals either with the targeted disease state or free of the particular disease under study and speeding the process of getting new therapies and medications to market remain serious endeavors. The mechanisms through which study subjects are recruited remain fragmented and uncoordinated.

[005] Clinical trials, which are used to assess the safety and efficacy of potential new diagnostics and therapies, now involve thousands of patients, take years to complete, and cost a great deal. The biopharmaceutical

industry spends hundreds of millions of dollars on patient recruitment for its clinical studies. It is a highly regulated, complex, and traditional industry that goes to extreme lengths to find individuals whose medical profiles fit the needs of specific clinical trials. The biopharmaceutical industry prides itself on its success, yet is always seeking new and productive channels of patient recruitment for its research.

[006] A variety of organizations have varying levels of access to samples or medical data from larger populations. These organizations, however, fail to meet the needs of the biopharmaceutical industry.

[007] Clinical Research Organizations (CROs) have access to patient populations with highly detailed medical records and longitudinal data (participants in Phase I trials often repeat). However, these patients lack ethnic diversity and are targeted to very narrowly defined and limited diseases not usually suitable for discovery purposes. To better characterize issues such as unforeseen toxicity events and non-responders, genomics-based investigation will require samples from larger and more diverse populations than those represented solely in current clinical trials.

[008] Diagnostic companies also have wide population access and some of them have growing genotyping capability. However, they have no long-term sample storage infrastructure. Additionally, these companies do not provide medical characterization, medical histories, or interaction with donors. Because of the lack of this interface, diagnostic companies are unable to sample the donors repeatedly or track their disease progression.

[009] Health Maintenance Organizations' (HMOs) primary shortfalls are that current records are claims-based, rather than medical records, and there are no samples associated with these records and no informed consent for the use of these data in research. While claims and pharmaceutical prescription data provide a privileged perspective of each patient, the medical information needed to monitor patient behavior, such as drug compliance or disease progression, resides with the physician, not the insurance provider. HMOs do not maintain a direct patient interface. Additionally, the perception that HMOs could possibly abuse genotyped samples to discriminate against

patients creates an environment that is not conducive to the collection of family histories, medical records and longitudinal samples.

[010] Life and disability insurers have single-time point medical data and do not store biological samples. Repeat access to medical data typically occurs only when an individual requests an increase in insurance coverage or makes a claim. Therefore, repeat access over time (*i.e.,* longitudinal access) and access to samples are missing from the insurance companies' capabilities. As is the case with HMOs, consent also is an issue for insurers since genetic disease proclivities might be used to discriminate against patients or alter their insurance rates. The claims data processed by insurance companies for statistical purposes do not include personal identifiers or names which could be used to solicit samples.

[011] Sample collectors and specialty blood banks, such as cord blood banks, have access to high quality samples suitable for genetic analysis. However, the samples are frequently collected outside of the context of diseases and are not connected to extensive medical records other than children's birth records. These are often one time samples with no repeat access or possibility for longitudinal analysis and may not have been collected with full disclosure or consent. Most of such specialty blood banks are local and do not draw from a large population base.

[012] Existing genetic population profiling companies, e.g., deCode genetics and Myriad Genetics, target well-defined, but usually inbred, populations in an effort to discover or validate genetic markers linked to disease. Additionally, the target populations tend to be restricted. For example, deCode genetics has access to the medical and genealogical records of the Icelandic population, albeit with only implied informed consent from the individual subjects. Similarly, Myriad Genetics has access to the genealogical records of Mormons in Utah. Neither company has significant access to subjects outside of the target population to verify that candidate genetic markers are relevant to the general population. An example of the misleading conclusions that can result from the use of these selected population datasets is the initial expectation, based on analysis of selected

populations that the BRCA1 mutation was involved in approximately 40% of breast cancers, whereas it is now known that BRCA1 plays a role in only 3%. Furthermore, diseases not prevalent at a high enough frequency in these restricted populations are not addressable.

[013] In contrast, collection establishments enjoy the goodwill and participation of nearly 100,000 individuals each business day. It is well known that blood and plasma donors seek the satisfaction of certain altruistic characteristics through the act of donating. In fact, the safety of a nation's blood supply is typically grounded in the goodwill and honesty of volunteers offering themselves as donors, responding truthfully to medical history questions about their health and certain risk factors in behavior, and the laboratory screening practices for viruses and other diseases known to be transmitted through a transfusion. On average, approximately 15% of those who approach a collection establishment to donate blood are deferred, either temporarily or permanently.

[014] The history of cooperation between the pharmaceutical industry and the blood and plasma industry is well documented, far-reaching, and comprehensive. Without a standing relationship between these industries, blood and plasma organizations would not be able to collect, test, document, and ship products; biopharmaceutical companies would lack significant sales. Professional industry seminars would not be held, nor would numerous physicians, scientists, technologists, and other professionals have access to the latest technology and science in blood and plasma collection and testing. Despite this history of cooperation, however, neither party has developed a method through which the pharmaceutical industry can utilize the sample and data collecting capabilities of the blood and plasma collecting industry to satisfy basic and clinical research needs.

[015] Summary of the Invention

[016] Systems and methods consistent with the present invention provide a new function for the process of donor management in regulated blood and plasma organizations, referred to herein as "collection establishments." To date, the sole purpose of the collection of ancillary blood

samples and personal medical information from blood and plasma donors has been to determine the safety of the procedure for both the donor and the eventual recipient. Most individuals who approach a collection establishment are accepted as donors. Some, however, do not meet the standards for acceptance and are deferred from donating, either on a temporary or on a permanent basis.

[017] Using databases and personal donor relationships conventionally directed toward donor and product safety, the instant invention provides a method through which the substantial data and sample collecting capabilities of collection establishments can be used to identify and recruit subjects for participation in clinical trials. Because collection establishments maintain contact with individual donors over an extended period of time, often years or longer, the invention provides methods through which these same capabilities can be used to identify genomic and proteomic factors that are correlated with the development of disease and/or the response of an individual to drug treatment.

[018] The processes contemplated are (1) the referral of select blood and plasma donors into clinical research studies; (2) the recruitment of blood and plasma donors into clinical research studies; (3) the collection of additional samples and data from donors for use in medical research; and (4) the development of a database comprising the bioinformatic analysis of donor medical histories and biological samples, which can be used to identify genomic, proteomic, and pharmacogenomic correlates of disease and therapeutic response.

[019] BRIEF DESCRIPTION OF THE DRAWINGS

[020] The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate implementations of the invention and, together with the description, serve to explain the advantages and principles of the invention. In the drawings, dashed lines represent optional elements.

[021] Figure 1 shows a flowchart of steps involved in processing donors from various sources to generate a clinical trial subject database, a

proteomics/genomics/pharmacogenomics database, and a database of biological samples in a manner consistent with the principles of the present invention;

[022] Figure 2 shows a flowchart for processing an end-user generated query to identify clinical trial subjects in the clinical trial subject database in a manner consistent with the principles of the present invention;

[023] Figure 3 is a diagram used to explain how repeated samples from individuals are preserved and tested, either prospectively or retrospectively, for genomic abnormalities and proteomic abnormalities. The disease status of the individuals also is monitored;

[024] Figure 4 shows a system in which methods and systems consistent with the present invention may be implemented; and

[025] Figure 5 shows the components of a desktop or a server computer of the system of Figure 4.

[026] DETAILED DESCRIPTION

[027] Systems and methods consistent withthe present invention provides methods that enable the biopharmaceutical industry to access a large and varied group of individuals whose medical data, for example, demographic characteristics, genetic markers, biochemical markers, family histories, and medical histories, make them attractive candidates for medical research to advance disease diagnostics and therapies. Such systems and methods use a network of non-profit and/or for-profit organizations and partners that have not traditionally been involved in this area of significant medical research as a source for such individuals. For example, a network of collection establishments refers deferred donors and, optionally, accepted donors, into specific clinical studies and collects blood samples and information from both deferred and accepted donors for pharmacogenomic, genomic, or proteomic studies under Institutional Review Board (IRB)-approved procedures and informed consents.

[028] Using systems and methods consistent with the present invention, entities conducting clinical studies have new access to an infrastructure of blood samples, personal medical information and individuals

free of specific diseases and those who may have a specific disease(s) under research. Because individuals often donate blood on a regular basis over long periods of time, *i.e.*, years, the methods of the invention permit the health of donors to monitored over an extended period of time and, furthermore, permit samples to be collected as an individual's medical condition changes.

[029] The ability to propose participation in clinical research to blood and plasma donors enables the biopharmaceutical industry to locate individuals whose disease state, medical histories, and patterns of compliance within a regulated industry result in greater speed through the regulatory approval process and the arrival in the marketplace of life-enhancing diagnostics and therapies for the nation.

[030] The pharmacogenomic interests of the biopharmaceutical industry can also benefit from using systems and methods consistent with the invention. For example, blood and plasma donors' blood and corresponding medical data are used in creating specific genomic and/or proteomic profiles that become benchmarks in the development of diagnostics or therapies for specific diseases. The company looking for the best candidates for a clinical trial on that disease, then focuses enrollment on patients whose profile fits the benchmark. Traditional large Phase III studies are made more efficient. This reduces the time and effort necessary to recruit large numbers of study patients and reduces the cost of drug development for many medicines.

[031] In one implementation consistent with the present invention the problem of recruiting subjects into clinical trials is addressed by providing biopharmaceutical companies with access to a large, diverse population of individuals with well-documented medical histories and detailed clinical profiles. Clinical trial subjects may be recruited from a variety of sources, including, but not limited to, deferred donors and individuals with specific diseases identified through partnerships with physicians and medical centers.

[032] Another implementation consistent with the present invention provides biopharmaceutical companies and researchers with access to a store of biological samples, including, but not limited to, whole blood, serum,

proteins isolated from blood and nucleic acids isolated from blood, obtained with informed consent from a large, diverse population of individuals with well-documented medical histories and detailed clinical profiles. Currently available methods for collecting biological samples from diseased and healthy individuals for genomic and proteomic studies do not reflect the general population because the samples are often from inbred populations with a small founder population. Furthermore, many of these samples are obtained without proper, active informed consent, which is becoming more and more of a concern as the general public becomes aware of the potential monetary value of genetic studies. At present, most readily accessible sample collections represent rather small numbers of individuals and lack the ability to follow-up with the donors through a carefully controlled system that ensures privacy of the donor.

[033] Yet another implementation consistent with the present invention facilitates the study of the inheritance of traits in the context of the entire DNA sequence complement of the organism, a branch of science known as genomics. In addition to analyzing the role of individual genes, genomics seeks to evaluate the importance of potentially highly complex interactions of multiple genes in health and disease. Of further interest is the investigation of an individual's response to treatment with a drug so as to correlate an individual's genetic makeup with drug effectiveness (or pharmacogenomics).

[034] It is believed that, on average, any two individuals differ by only 0.1% in the approximately 3 billion base pairs that make up the genome. This, however, represents as many as 3 million differences, or polymorphisms. In most instances, these polymorphisms represent single base differences, and are thus known as single nucleotide polymorphisms (SNPs). Most of these 3 million or so SNPs lie outside of genes, which comprise only about 3% of the genome, and, in most instances, have no effect on the individual. Even for SNPs that lie within genes, most have no effect on the protein encoded by the gene because of the degeneracy of the genetic code. Benign or silent SNPs, however, may be useful if they co-

segregate with a disease phenotype or if they indicate a specific response to drug therapy.

[035] In some cases, the study of linkage or association of certain genetic markers with the disease state in well-characterized populations has enabled identification of a single gene defect that is both necessary and sufficient for manifestation of the disease. It also has been proven invaluable to have DNA samples from individuals with such so-called monogeneic disease, together with samples from genetically related individuals who do not show signs of the disease. Success also has been seen with populations of well-characterized, unrelated, individuals and matched controls.

[036] The majority of common diseases, however, are rather more complex and are believed to result from the contribution of variations in a number of genes. The combination of certain mutations or polymorphisms can lead to a predisposition to develop a disease, though it is clear that environmental factors also contribute in many instances. In order to understand the etiology of these complex diseases, it is believed that the best approach is to collect large epidemiological study samples from many different populations (Peltonen *et al.*, Science 291: 1224-1229, 2001). One implementation consistent with the present invention facilitates the collection of such large numbers of samples across a varied population.

[037] The study of the human genome has further shown that there may be as few as 30,000 genes in the genome and, therefore, that much diversity must be provided through differences in the synthesis of messenger RNA and, subsequently, protein in different tissues. Consequently, it is important to be able to study the differences in the protein complement of individuals (the proteome) or changes in the posttranslational modification of proteins (both encompassed by the term "proteomics"), particularly any differences between healthy and diseased individuals. Unfortunately, while collections of samples from diseased individuals exist (though often without appropriate informed consent), there are generally no matching samples from those individuals prior to the development of the disease state, which severely limits the types of analysis that can be performed.

[038] Another implementation consistent with the present invention facilitates the identification of such differences in protein expression between healthy and diseased individuals by providing samples from matched groups of healthy and sick individuals. By enabling the provision of large numbers of samples, techniques based on the pooling of samples from one or more groups of individuals can become particularly powerful. Still another implementation consistent with the present invention allows the proteomes of single individuals to be compared before and after disease development. And in a further embodiment, changes in the posttranslational modification of proteins can be investigated in healthy and diseased states.

[039] Yet another implementation consistent with the present invention comprises a longitudinal database in which medical and demographic information for each donor, whether obtained through a collection establishment or through partnerships, is linked to genomic data for that donor, obtained, for example, through SNP analysis, and proteomic data for that donor, obtained, for example, through the analysis of the donor's proteome. These data are correlated with the subject's disease status and stored in a proteomics/genomics database. The samples collected from an individual over time for example, from that individual's first sample donation through either the development of disease in or death of that individual, also are stored and may be retrieved by accessing a longitudinal database of samples. The database may be queried in order to identify genomic and/or proteomic changes associated with the development of disease. Furthermore, as the database comprises vast amounts of data from large numbers of individuals, researchers are able to query the database in a hypothesis-free manner, as well as with hypothesis-driven queries. For instance, the vast amount of data can be queried for unexpected correlations of certain genomic and proteomic characteristics with disease phenotypes.

[040] Another implementation consistent with the invention facilitates drug target identification and validation. Traditionally, potential drug targets have been identified on the basis of hypotheses from biochemical or pharmacological study of the disease state. Genomics allows the expansion

of this approach to include searching the genome for genes encoding proteins with particular characteristics, or motifs, suggestive of classes of receptors or other classical drug targets or the study of changes in the expression of different nucleic acids. Alternatively, analysis of DNA samples for patterns of SNPs can be used to determine whether certain genotypes are associated with a particular disease, which may in turn lead to the identification of a new drug target. This latter approach requires samples of DNA from subjects with the target disease, together with a matched set of "healthy" controls.

[041] Yet another implementation consistent with the invention facilitates research into the individual variability in response to drug treatment, which is a consequence of the genomic make-up of the individual. The study of this variability in response to drugs and its relation to the genetic markers (SNPs) in an individual provide the opportunity for selection of the most appropriate treatment, in terms of both efficacy and safety. This approach, known as pharmacogenomics, plays an increasingly important role, not only in the selection of the most appropriate treatment for an individual, but also in drug development by enabling the selection of the most appropriate subjects for clinical trials.

[042] Reference will now be made in detail to implementations consistent with the present invention as illustrated in the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings and the following description to refer to the same or like parts.

[043] Definitions

[044] The term "collection establishment" as used herein refers to any blood or plasma organization contemplated as part of the invention. Collection establishments are typically regulated by the Food and Drug Administration or a similar agency. A collection establishment can be either an independent entity or owned by the contractor.

[045] The term "end-user" as used herein means any entity that requests the names of donors or deferred donors fitting the profile for clinical trial subjects. End-users also include any entity that orders blood and/or DNA

samples from a collection establishment for pharmacogenomic purposes and any entity that uses the longitudinal database of genomic/proteomic information.

[046] The term "contractor" as used herein refers to an entity that acts by contract as an intermediary between collection establishments and end-users. A contractor may be an end-user. The contractor queries collection establishments for individuals or samples that meet the criteria established by an end-user and arranges the supply of contact information or of those samples to the end-user. The contractor also provides end-users with access to databases according to the invention. The contractor may audit end-users to ensure the proper use of the information or samples by the end-user under the terms of the contract. The contractor's role as an intermediary does not preclude the contractor from undertaking additional functions of the invention including, but not limited to, sample preparation, storage, and shipping, SNP analysis, and proteomics analysis.

[047] The term "donor" as used herein means an individual who offers to donate or sell blood, plasma, or serum to a collection establishment. Donors fitting particular profiles also may be identified through partnerships with physicians, medical centers, and other health care providers.

[048] The term "deferred donor" as used herein means an individual who offers to donate or sell blood, plasma, or serum to a collection establishment, but whose offer is refused, either temporarily or permanently, based on medical history or other relevant information.

[049] The term "longitudinal" as used herein means obtained over a period of time. When the term "longitudinal" is applied to an individual or group of individuals, the period of time, in general, extends from an individual's first to last sample donations. The last sample donation may occur, for example, when the individual develops a disease, when the individual begins treatment of a disease, or upon the death of the individual. When the term "longitudinal" is applied to a sample or to information, the period of time may extend beyond the death of the individual from whom the sample or information was gathered.

[050] As used herein, the term "pharmacogenomics" pertains to the correlation between an individual's response to treatment with a drug and that individual's genetic makeup. The term may be encompassed within the more general term "genomics".

[051] Overview of System Components and Operation

[052] The implementation consistent with the invention may comprise a contractor, a network of collection establishments and, optionally, partners, and end-users. As exemplified below, systems consistent with the invention may be implemented using a computer network. Those skilled in the art will appreciate, however, that a manual implementation also may be consistent with the present invention. Systems consistent with the present invention enable end-users, for example, biopharmaceutical industry consumers, to select clinical trial participants, DNA samples, and tissue samples from subjects suitable for drug development studies and clinical trials. Suitable subjects will vary from study to study and may be selected based on criteria such as age, sex, ethnicity, or race. The skilled artisan will recognize, of course, that many other selection criteria also may be appropriately applied depending on the particular requirements of the study.

[053] Donor Information And Sample Collection

[054] As diagrammed in Figure 1, multiple collection establishments 101, 105, and 110 are intake sites for prospective donors 125, optionally in collaboration with one or more partners 115 and 120. The collection establishments obtain informed consent 127 from prospective donors in compliance with Institutional Review Board-approved procedures permitting, for example, the use of donated tissue samples in biomedical research and/or the release of the information needed to contact an individual to pharmaceutical companies seeking clinical trial subjects or research subjects. The collection establishments also collect donor demographic information, family histories, and medical histories 140 and 145, and, optionally, perform clinical chemistry analyses on donor samples 150 (any and all such information being generally defined as "medical data"). Table 1 provides examples of the type of information requested from prospective donors and

the types of clinical tests performed on the blood of prospective donors. A non-exclusive list of other possible tests, which may be performed either singly or in various combinations, are included in an Appendix .

Table 1

Demographic Information
- donor name
- donor social security number
- donor address and zip code
- donor phone – work and home
- donor birth date
- donor race
- donor gender
- donor employer

Donation Profile
- date of last donation
- total number of donations
- blood (ABO/RH) type

Health History
- weight
- temperature
- pulse
- blood pressure
- hemoglobin/hematocrit
- recent flu
- recent cold
- recent sore throat
- skin problems
- rashes
- any immunization
- chest pain
- heart disease
- lung disease
- cancer
- blood disease
- bleeding problem
- yellow jaundice
- hepatitis
- malaria
- Chagas disease
- babesiosis
- under a doctor's care
- recent surgery
- recent dental work
- taking any medication
- taken human growth hormone
- taken Tegison
- taken Accutane
- taken Proscar
- syphilis
- gonorrhea
- pregnant
- blood transfusion
- organ transplant
- tissue transplant
- tattoo
- ear or skin piercing
- contact with another's blood
- exposure to hepatitis
- exposure to Creuzfeldt-Jacob disease
- used a needle to take drugs
- given money for sex
- given drugs for sex
- taken money for sex
- taken drugs for sex
- sex with someone who has taken money for sex
- sex with someone who has taken drugs for sex
- men – sex with a man since 1977
- women – sex with a male who had sex with a man since 1977
- taken clotting factor concentrate
- sex with someone who has taken clotting factor concentrate
- AIDS
- positive test for AIDS
- sex with someone who has AIDS
- sex with someone who has HIV antibody
- travel outside U.S. or Canada
- born or lived in African countries since 1977
- received blood transfusion in African country
- had sex with someone from African countries
- transfusion-associated AIDS
- transfusion-associated Hepatitis

Laboratory Screening Tests

- antibody screening results
- alanine aminotransferase (ALT)
- Cytomegalovirus (CMV) screening
- Hepatitis B screening
- Hepatitis B Core Antibody screening
- Hepatitis C screening
- Human immunodeficiency virus (HIV) Types 1 & 2 screening
- Human T-cell lymphotropic virus (HTLV)-1 screening
- HIV Antigen screening (9)

Additional data maintained on plasma donors

- breastfeeding now
- close contact with someone with jaundice
- Varicella-Zoster (live)
- Hemophilus Influenza type B-
- PCR test (HAV, HBV, HCV, HIV, Parvovirus B 19)
- Serum protein electrophoresis (SPE)
- tetanus
- prison or jail in past 12 months
- atypical Anti-D Antibody
- antibiotics within the past 14 days
- urinalysis

[055] Additional information of use to the end-user may be collected, either prospectively or retrospectively. One skilled in the art will readily recognize that the nature of the donor information requested is dictated by the requirements of the study in which the donated sample is to be used.

[056] The information collected is gathered by any available mechanism, including, but not limited to, confidential, personal interviews, the use of self-executed forms, or even by direct entry into a computerized database, for instance via a personal computer terminal or via a hand-held device. The information collected from prospective donors may be generally the same as is collected at present by collection establishments and is maintained in confidence.

[057] The existing infrastructure of the blood and plasma industry may be employed to collect information from donors. Individuals collecting information are trained to comply with Standard Operating Procedures (SOPs) developed for the business. The training of individuals responsible for collecting donor information is documented and entered into the individual's permanent personnel record. Individuals collecting information from donors are located either at the site of the collection establishment or at one or more remote locations separate from the point of contact for blood and plasma donors. These individuals also are equipped to explain and administer informed consents. The informed consent describes, for example, the fact that information of a personal and/or familial nature is requested by an end-user, for example, a pharmacogenomic, biotechnology, or pharmaceutical company, developing treatment or drugs to help cure specific diseases. If the nature of the disease to be studied is known, this information may be disclosed in order to engage the interest of the donor.

[058] Informed consents are maintained by the collection establishments, or, alternatively, by a contractor, preferably in donor files. It is not contemplated that the names or informed consents of individual donors are disclosed to clients. Rather the collection establishment provides the client with evidence of informed consent, for example, a Verification of a

Signed Informed Consent Form accompanying donor-derived samples. If desired, audits performed at the request of the client and, preferably, conducted by an independent third party, assure the client that proper informed consents have been administered. In addition, since most of the data collected from donors is entered into a computer, all appropriate firewalls of confidentiality and privacy are, of course, employed. The signature for the Informed Consent may be implemented using digital signature techniques.

[059] To further protect the identity of donors, the invention employs alphanumeric strings, rather than names, to identify each donor. Such strings may be assigned by either the contractor, the collection establishment, or the client. The collection establishment may assign unique, confidential identification numbers to donors. The collection establishment may also assign a unique, confidential identification number to each sample collected from a donor. Presently, a unique one-time number is assigned to the product donated in both the whole blood and the plasma industries. In implementation consistent with the invention, these numbers are used to identify sample and donor information.

[060] Based on the prospective donor's answers and test results, the individual is classified either as an accepted donor 130 or as a deferred donor 135. Medical history and clinical testing data along with the results of proteomic and genomic analyses of both accepted and deferred donors are combined to make the proteomics and genomics database 155.

[061] The clinical trials database 160 comprises data collected from deferred donors. Optionally, the clinical trials database also may comprise data collected from accepted donors

[062] Data collected from donors are kept in perpetuity. As requested by an end-user and in compliance with an IRB-approved informed consent, donors are, from time to time, asked to supply additional and/or updated information. All such updates are incorporated into the permanent record of the donor.

[063] Method For Identifying Clinical Trial Subjects

[064] One implementation of the invention provides a method for identifying a research subject, comprising: a) obtaining medical data from a subject; b) associating an identifier for said subject with said medical data in at least a first database; c) associating the identifier for said subject with the name and contact information of said subject; d) identifying criteria for selecting a research subject; e) extracting an identifier from the first database, wherein said identifier is associated with a subject matching the identified criteria; and f) matching the identifier from the first database with the name and contact information in order to identify the research subject.

[065] A request to identify potential clinical trial subjects originates with an end-user 201 (see Figure 2). The end-user provides desired subject characteristics 210 to the contractor 215. For example, the end-user may wish to identify individuals with specific pharmacogenomic characteristics, e.g., relating to a cytochrome P450. Based on those characteristics, the contractor formulates a query 220, which is designed to interrogate the clinical trials database 160 for subjects with the desired characteristics. The query is sent to Server A, which comprises the clinical trials database, over a communications network 230. Records in that database that satisfy the query are identified 240 and output as unique patient identifiers by Server A 250.

[066] In one implementation consistent with the invention, the name and contact information associated with each identifier also are stored in the clinical trials database 160.

[067] In another implementation consistent with the invention, the name and contact information associated with each identifier are stored in a second database, which cross references the unique patient identifiers with the names and contact information of the corresponding individuals.

[068] In one implementation consistent with the invention, the clinical trials database and the second database are stored on Server A. In another implementation, the second database is stored on a separate Server B 270. In implementations of the invention utilizing Server B, Server A may be either directly linked to Server B through a firewall 260 or, alternatively, freestanding

and without links to other components of the communications network. Information is retrieved from Server B either through the communications network if a link is present in the system or manually if Server B is freestanding.

[069] In general, the contractor or the collection establishment contacts individual identified and seeks permission to pass patient contact information 280 on to the end-user. Alternatively, the patient information 280 may be sent directly to the end-user, who then contacts the individuals identified or, alternately, further refines the query for resubmission to the contractor.

[070] Although the invention does not contemplate directly releasing data, other than names and contact information, supplied by individual donors to end-users, donors are, on occasion, asked for permission to release demographic information. Such demographic information is only released in confidence to end-users and without disclosing the identity of the individual(s) from whom that information was collected. Additionally, from time to time, and with donor consent, the results of donor testing for viruses, including, but not limited to, hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV), are disclosed to end-users.

[071] Method For Establishing A Proteomics/Genomics Database

[072] As illustrated in Figure 1, biological samples 150 are collected from both accepted and deferred donors. The sample collected is generally whole blood, but other tissues may be collected, especially in collaboration with partners. Portions of each sample are stored as whole blood or as any fraction of whole blood (e.g., serum, lymphocytes, erythrocytes, etc.) and as nucleic acids derived from such whole blood or fraction of whole blood. Donor DNA and RNA are extracted using methods, either manual or automated, known to those skilled in the art.

[073] Donor samples are stored under standard conditions known in the art, preferably at a centralized depository maintained by the contractor, although storage at multiple sites, which may be maintained by third parties, is consistent with the invention. In one embodiment, stored samples are bar-

coded with unique identifiers to facilitate their identification and retrieval from storage. The facility for sample handling and storage may include a system for robotic handling and retrieval of individual samples.

[074] As illustrated in Figure 3, samples 301, 311, 321, 331, 341, and 351 are collected from the same individuals repeatedly over time, in general over years. These samples are stored as described above and constitute a longitudinal sample database 305. The longitudinal sample database comprises at least 2 samples, and may comprise at least 50, at least 1000, at least 10,000, at least 500,000, at least 1,000,000, at least 5, 000,000, or at least 10,000,000 samples. Samples are retrieved from the longitudinal sample database on demand to satisfy the needs of the contractor or of an end-user.

[075] In addition to the data in Table 1 and, optionally, additional information from other tests, for example, listed in the Appendix,, which are associated with each sample, genomic experiments 312, for example, to detect SNPs or to monitor changes in gene expression, and proteomic experiments 315, for example, to detect aberrant protein expression or changes in the posttranslational modification of proteins, are performed on each sample either at the time the sample is acquired or retrospectively, for example to search for changes in DNA sequence, RNA expression, or protein activity that are associated with a later-arising disease 318.

[076] An example of information that may be stored in the proteomic/genomics database is shown in Figure 3. Assays performed on samples 301 and 311, which are collected from the same individual at different times, show a DNA polymorphism (e.g., a SNP), but show normal RNA and protein expression. At the times samples 301 and 311 are collected, the individual shows no sign of disease. Assays performed on samples 321 and 331, again collected from this individual but at later times, as before show a DNA polymorphism and now also show abnormal expression of at least one protein and/or RNA. The amount of abnormal expression increases between the date sample 321 is collected and the date sample 331 is collected. At the time sample 341 is collected, the individual

has begun to show disease symptoms. The DNA polymorphism persists and the extent of abnormal protein/RNA expression has increased. The DNA polymorphism persists in sample 351, but the abnormal protein and/or RNA is more or less abundant. Disease severity has worsened at the time sample 351 is collected, suggesting that the DNA polymorphism and the expression abnormality may be diagnostic for the disease and may be therapeutic targets.

[077] Databases

[078] Donor information and data associated with samples (e.g., storage location, SNP profile, etc.), collectively "information," may be stored using any method that permits high productivity, scalability, flexibility, accessibility, security, correctness and consistency of housed data, data granularity, and presentation. The storage system may be a computerized database. In one implementation consistent with the invention, the information is stored in a secure, computerized data warehouse system, accessible only by controlled passwords assigned to trained users. In general, collection establishments currently use this type of system for data storage. The data warehouse is designed using dimensional modeling, a logical design technique that seeks to present the data in a standard framework that is intuitive and allows for high-performance access. This type of modeling provides the optimal balance among critical factors such as productivity, scalability, flexibility, accessibility, security, correctness and consistency of housed data, data granularity, and presentation.

[079] A centralized database of information is generally maintained by the contractor, although systems for housing all or part of a database may be distributed at different sites.

[080] In one implementation consistent with the invention, end-users provide the contractor with criteria through which the desired donors and samples may be identified. The contractor causes the donor data and sample information database or databases to be searched using queries developed using the client-supplied criteria. Standard query protocols are used, resulting in the data required for the end-user. In general, a query tool

set is selected that allows for services such as warehouse browsing, query management, standard reporting, access and security.

[081] Database queries are performed by trained employees either of the contractor or of the collection establishments. Database queries may be performed by the contractor, by employees of the collection establishments, who, as part of their normal jobs, query the databases for routine purposes of the collection establishments, or by end-users, following protocols establishing confidentiality and proper security. The result of a query is the approach to an individual donor to participate in a client's research, the shipment of sample to the client, or the identification of desired proteomic/genomic information.

[082] It will be appreciated that the present invention may be implemented in a software system, which is stored as executable instructions on a computer readable medium accessible either directly or through a network. Figure 4 illustrates a conceptual diagram of a computer network 400 in which methods and systems consistent with the present inventionmay be implemented to permit users to query a database of donor and sample information. Computer network 400 comprises one or more small computers (such as desktop computers , 410, 420, and 425) and one or more large computers (such as Server A 412 and server B 422). In general, small computers are "personal computers" or workstations and are the sites at which a human user operates the computer to make requests for data from other computers or servers on the network. Usually, the requested data resides in the large computers, but the size of a computer or the resources associated with it do not preclude the computer's acting as the home of a database. In one implementation consistent with the invention, Servers A and B are connected through a firewall 435, which permits secure access to information that identifies donors to authorized users. In another implementation consistent with the invention, Servers A and B are not connected by a network and patient information must be accessed directly from server B.

[083] Desktop computer systems and server systems compatible with the invention includes conventional components, as shown in Figure 5, such as a processor 524, memory 525 (e.g., RAM), a bus 526 which couples processor 524 and memory 525, a mass storage device 527 (e.g., a magnetic hard disk or an optical storage disk) coupled to processor 524 and memory 525 through an I/O controller 528 and a network interface 529, such as a conventional modem or Ethernet card.

[084] The distance between a server 412 and a desktop computer 410 may be very long, e.g., across continents, or very short, e.g., within the same building. When the distance is short, the network 400 is preferably a local area network (LAN). When the distance between server 412 and desktop computer 425 is long, the network 400 may, in fact, be a network of networks, such as the Internet. In traversing the network, the data may be transferred through several intermediate servers and many routing devices, such as bridges and routers. Proper security and flexibility of access will be employed to provide authorized access through commonly used interface technologies.

[085] The software system of the present invention is, for example, stored as executable instructions on a computer readable medium on the desktop and server systems, such as mass storage device 527, or in memory 525. Access to the system described above is available on a single-use or on a multiple-use basis. Preferably, end-users contract with the contractor for continuing access to the system.

[086] The foregoing description of implementations of the invention has been presented for purposes of illustration and description. It is not exhaustive and does not limit the invention to the precise form disclosed. Modifications and variations are possible in light of the above teachings or may be acquired from practicing of the invention. For example, the described implementation includes software but the present invention may be implemented as a combination of hardware and software or in hardware alone. The invention may be implemented with both object-oriented and non-

object-oriented programming systems. The scope of the invention is defined by the claims and their equivalents.

APPENDIX

1,1,1-Trichloroethane, Blood
1,25-Dihydroxy Vitamin D3
11 DEOXYCORTISOL
11-Desoxycortisol
17-Hydroxycorticosteroids
25-Hydroxycalciferol
3-A-ANDROSTANEDIOL
3-Methoxy-4-Hydroxymandelic Acid
4-AMINOANTIPYRINE
5' Nucleotidase
5-HIAA
5-NUCLEOTIDASE
5T Allele Genotyping
A, Vitamin
A-1 Apolipoprotein
A1A Phenotyping
A1-Antitrypsin
A-1-ANTITRYPSIN
Abnormal Bleeding Profile
ABO
ABSCESS AFB CULTURE
AC Globulin
ACA
ACE
ACH R AB
Acid Anhydride Profile
ACT LOW RANGE-MEDTRONIC
ADENO AG BY DFA
ADH
ADRENAL ANTIBODIES
ADVIL
AEROBIC CULTURE
AFB BLOOD CULTURE
AFP
AGBM
ALA
Albumin
ALCOHOL PANEL
ALDOLASE
Alk Phos
ALPHA 2 ANTIPLASMIN
ALT
ALUMINUM
AMA
AMIKACIN
AMMONIA
AMNIOTIC FLUID
AMOBARBITAL
AMPHETAMINE
AMYLASE

APPENDIX

ANA
ANCA
ANDROSTENEDION
ANGIOTENSIN CONVERTING ENZYME
ANTI GBM
APC Mutations in FAP
APOLIPOPROTEIN A1
APTT
ARGININE VASOPRESSIN
ARSENIC
ASCORBIC ACID
ASMA
ASO (ANTI-STREPTOLYSIN O) TITER
ASPARTATE AMINOTRANSAMINASE
AST
AT III
a-Thalassemia
AURAMINE STAIN
AUTOMATED DIFFERENTIAL
AVP
B CELL CYTOTOXIC CROSSMATCH
B SURFACE ANTIGEN
B VIRAL DNA
B.PERTUSSIS CULTURE
B1 Vitamin, Plasma
B12
B-19 PCR
B27
B2-MICROGLOBULIN
B6, Vitamin
Bacterial Antigens (Serum, Urine, Cerebrospinal Fluid)
BAL FOR CMV CULTURE
BANDS
BARBITAL
Basic Metabolic Panel
BAYER ENCORE QA PLUS, GLUCOSE
BB
B-Cell Gene Rearrangements, Ig Heavy Chain
BCL-2 t(14;18) Translocation
BCR-ABL t(9;22) Translocation
BCSF
BENADRYL
Beta Apolipoprotein
Beutler-Baluda Test
BGP
B-hCG Quantitative, Serum
Bi, Blood
BICARBONATE
Bile Acids
Bioavailable Testosterone

APPENDIX

BISCODYL
Bladder Tumor Antigen (BTA) Cytology Profile
BLEEDING TIME
Blood Acetone
BODY FLUID
Bone Alkaline Phosphatase (BAP)
BORDETELLA PERTUSSIS CULTURE
BRAIN BIOPSY
Breast
BROMPHENIRAMINE
BRUCELLA AGGLUTININ
BSAB
BSF-2
BTA
b-Thalassemia (Cooley's Anemia, Mediterranean Anemia
BUFFY COAT FOR CMV
BUN
BUPROPION
BUTABARBITAL
C, Vitamin
C. DIFF TOXIN
C.DIFF CULTURE
C1 Esterase Inhibitor
C1EI
C1Q
C2 Complement
C3
C3c
C4
C4, Body Fluid
Ca
Ca, Urine
Ca++, Ionized, Serum
CA-125
Cachectin
CADASIL
CAE
CAFFEINE
CALCITONIN
cAMP, Urine
Canavan Disease, DNA Analysis
C-ANCA-Specific Antibody
Cancer Antigen (CA) 125
CARBAMAZEPINE
CATECHOLAMINES
CBAVD
CBC
Cd, Blood
CD25
CD3

APPENDIX

CD4
CD8
CDF
CEA
Celiac Disease (CD) Antibodies
Centrax®
c-erbB-2
CEREBROSPINAL FLUID (CSF) CULTURE
CF Carrier
CH50
Chain-of-Custody Protocol, Specimen
CHEM 10
Chickenpox Culture
CHLAMYDIA
Chol
Christmas Factor
Circulating Anticoagulant
CITRATE
CK
CK, Serum
CK-2
Cl
Cl, CSF
CLB Smear
Clearance, Creatinine
Clomipramine (Anafranil®), Serum
CMV
CO, Blood
CO2
COAG FACTOR CONCENTRATES
Cobalamin, True
COCAETHYLENE-COCAINE ANALOG
Codeine
Coke
Cold Agglutinin Titer, Quantitative
Combined Esterase (CES)
COOMBS CROSSMATCH
COPPER
CORD ISOHEMAGGLUTININS
COTININE
Coumadin®
Coxiella burnetii Antibodies
C-PEPTIDE
CPK
CPPT
Cr, Plasma
Crack
C-REACTIVE PROTEIN
Creat
CRM Assay

APPENDIX

CROSSMATCH TEST EA UNIT
CRP
CRYO
CSA
CSF AFB CULTURE (SpinalFl)
cTnI
Cu, Plasma
CULTURE FOR B.PERTUSSIS
Cutaneous Immunofluorescence, Indirect
CVS Prenatal Karyotyping, Chromosome Analysis
CYANIDE
CYCLIC ADENOSINE MONOPHOSPHATE
Cyst Fluid Amylase
CYTOLOGY, "RUSH" OR "SAME DAY"
D
D Factor
D XYLOSE 5 HOUR TOLERANCE URINE
DALA
DANTHRON
DARKFIELD EXAM
DAT
DAZ+ Analysis
DBili
DCC Allelotyping
D-DIMER
DDT Exposure Profile
DEHYDROEPIANDROSTERONE
DELTA
DEMEROL
DEOXYCORTICOSTERONE
DEPAKENE
Dermatophyte Culture
DES
Dexedrine®
DFA FOR CHLAMYDIA
DHEA
DHT
Diazepam, Serum
DIBUCAINE
DIC Profile
DIFF
Digitalis
Dihydrotestosterone
DIL
Dimethylacetamide Exposure Profile
DIPHENHYDRAMINE
DIRECT ANTIGLOBULIN
Disease Association
DITHIONITE TEST
DMAC

APPENDIX

DMD/BMD
DNA Analysis for Parentage Evaluation
Dolophine®
DOPAMINE
DORIDEN
DOUBLE-STRANDED DNA
DOXEPIN
Dpd
D-PYRALINKS
DQ1
DR Transplant
DR2
DRAINAGE CULTURE
DRVVT
DS-DNA
Duraquin®
d-Xylose Absorption Test
E. coli O157:H7
E.HISTOLYTICA CULTURE
E1
E2
E3, Serum
Ear Culture
EBV
ECG Cardiologist Overread Only, Adult
ECTODERMAL DYSPLASIA (LINKAGE ANALYSIS)
ED STAT PANEL A
Effusions Cytology
EGFR
EHEC, Stool Culture
ELAVIL
Electrolyte Panel
ELISA ANTIBODY SCREEN
ELUTION
ELVIS®
Endep®
ENGRAFTMENT STUDY
ENTAMOEBA HISTOLYTICA CULTURE
Environmental Culture
Eos Count
EP
EPG SERUM
EPHEDRINE
Epidermal Growth Factor Receptor (EGFR)
EPO
Epstein Barr Virus (EBV) Antibodies
ER/PR Assay
Erythrocyte Count
Eskalith®
ESOPHAGEAL BRUSHING CYTOLOGY

APPENDIX

ESR
Essential and Metabolic Fatty Acids Analysis
Esterase Inhibitor
ETHANOL (NOT FORENSIC)
EtOH
Etrafon®
Excedrin®
Extrinsic Factors
Eye
F, Plasma
FA FOR B.PERTUSSIS
Factor B
Familial Adenomatous Polyposis (FAP)
FANA
FAP Analysis, Known Mutation
Farmer's Lung
Fast Hemoglobins
FAT STAIN
FBS
FDP, Plasma
Fe
FECAL CULTURE
FELBAMATE
Female Hormone
FEP
FERN TEST
FETAL FIBRONECTIN
FFP
FIBRIN SPLIT PRODUCTS
FINE NEEDLE ASPIRATE CYTOLOGY
FIORNAL
FISH
FK506
FK-506
FLECAINIDE
FLOW ANTIBODY SCREEN
FLU A
FMR-1 Gene Trinucleotide Repeat Analysis
FOLATE
Fourth Complement Component
FPL
Fractionated Amino Acids, 24-Hour Urine
Free and Albumin-Bound Testosterone
Friedreich Ataxia (FRDA)
FROZEN PLASMA
Fructosamine
FS
FSH
Ft Bragg Fever
FT4

APPENDIX

FTA-Ab
FULL CROSS
Functional Protein C
G-1-PUT
G6PD
G-6-PD QUANTITATIVE
GABAPENTIN
GAD AUTOANTIBODIES
GALACTOSE
GAMMA GLUTAMYL TRANSFERASE
GANGLIOSIDE GM1 ANTIBODIES
Garamycin®
Gastric Analysis
Gaucher Disease, DNA Analysis
GC (Neisseria gonorrhoeae) Culture Only
GENERAL VIRAL CULTURE
Germ Cell Panel
Gestational Diabetes Evaluation
GGT
GHB
GIARDIA FA
GIEMSA STAIN
Glass Activation Factor
Gliadin Antibodies
Globulins, 24-Hour Urine
Glu
GLYCATED ALBUMIN
GM1 ANTIBODIES
GM2 Gangliosidosis
GMS/FUNGAL SILVER STAIN
Gonorrhea Culture
Goodpasture Syndrome
GOT
GPT
GRAM SMEAR, DIRECT
Gross and Microscopic Pathology
GT
GTT
Gynecologic Pap Smear and Maturation Index
H and E Sections
H. FLU GROUP B LATEX AGGLUTINATION
H.PYLORI AB
H2 RECEPTOR ANTAGONIST
H2a/H2b and H3 and H4 Antibodies
HAA
Haemophilus influenzae B Antigen
Hageman Factor
Hairy Cell/Plasma Cell Leukemia Profile
Haldol®
HAMA

APPENDIX

HANE Assay
Haptoglobin
HAV/HBV (Profile VII)
Hb A1c
HBcAb, IgG/IgM Diff
HBeAb
HBSAB
HBV DNA Qualitative PCR
HCG
HCT
HCV Ab (Immunoblot Reflex)
HDL
HDV
Heat Precipitate Fibrinogen
HEINZ BODY STAIN
Helicobacter pylori Antibodies
Hema-Chek®
HEP AM
HER-2/neu Gene Amplification
Heterophil Agglutinins
Hexagonal Phase Phospholipid
Hg, Blood
HGB
HGF
HGH
HHV-6, IgG
High Resolution G-Banding
HIPA
Hirsutism Prof, Comprehensive
HISTAMINE
HITS
HIV
HLA A Typing
HNPCC, Direct, Known Mutation
Hog
HOLD SPECIMEN
Homocyst(e)ine, Plasma or Serum
Hormonal Evaluation Cytology
HPV
HS CRP
HSF
HSV
HTLV
Human Antimouse Antibodies
HUNTINGTON DISEASE MUTATION
HVA
Hybrid Capture
Hyperhomocysteinemia, C677T Mutation
IA2 Antibodies
IA-9

APPENDIX

IAA
IBC
IBUPROFEN
ICA512 Autoantibodies
ICSH
Ictotest®
Identification of Atypical Bacteria
IFE/Protein Electro, 24-Hr Ur
Ig Heavy Chain Gene Rearrangement
IGA
IgD
IgE
IGF BINDING PROTEIN 3
IGG
IGM
IL-2 sR
Imavate®
IMIPRAMINE
IMMEDIATE SPIN CROSSMATCH
In situ Hybridization for HPV
Inborn Errors of Metabolism
Inclusion Body Stain
INDIA INK (SpinalFl)
INFECTIOUS MONO
Inherited Mental Retardation
Inorganic Phosphate, Blood
INR
Insulin
Interleukin-2 Receptor
IONIZED CALCIUM
IRON
IS CROSSMATCH
ISLET CELL ANTIBODY
Isoagglutinins
ITRACONAZOLE LEVEL
IVY BLEEDING TIME
Ixodes Tick Bite Agent
Jembec Culture
Jewish Heritage
JO 1
JOINT FLUID
JUMBO FFP
K
K
K and L Chains, Urine
Kappa Light Chains, Urine
Karyotype
KENNEDY DISEASE DNA

APPENDIX

Ketone Bodies, Serum
Ki67
Kidney Stone
Killer Weed
KLEIHAUER-BETKE
KlonopinTM
KOH
L/S Ratio
Labile Factor
Lactate
Lambda Light Chains, Urine
Lanoxin®
LAP
LASA
Latex
LAXATIVE ABUSE SCREEN
L-Carnitine, Total, Free, and Esters
LCM
LD
LD, Body Fluid
LDH
LDL
LEAD
Lecithin/Sphingomyelin Ratio
Legionella Antibodies, IgM
LEISHMANIA CULTURE
LEPTOSPIRA CULTURE
Lesion Culture
Leu3A
LGV
LH
LHRT
Li, Blood
Librax®
LiCO3
LIDOCAINE
Li-Fraumeni Syndrome (p53)
LILEY CURVE, AMNIOTIC FLUID
LIPASE
Liquiprin®
LITHIUM
Liver Cancer Monitor Profile
LKM-1 Antibodies
Loa loa Smear
Long chain 3-hydroxyacyl-CoA dehydrogenase
LORAZEPAM
Loss of Heterozygosity
Low-Density Lipoprotein Cholesterol (Direct)
LOXAPINE
LP

APPENDIX

Lp(a)
LRP
LSD Screen, Urine
LUKENS-TRAP
Lumbar Puncture
Lung, Adenocarcinoma Monitor Profile
Lupus Anticoagulant
Luteinizing Hormone (LH) and (FSH)
Lyme Disease (Borrelia burgdorferi) by PCR
Lysergic Acid Diethylamide, Urine
M PNUEMONIA ANTIBODY
MAC BLOOD CULTURE
MAGNESIUM
MAI BLOOD CULTURE
MALARIA
Manganese, Blood
MAPROTILINE
Marijuana
Maternal Serum Alpha-Fetoprotein
MAXIMUM BACTERICIDAL DILUTION
MBC
MBD
MBK, Blood
MBP
MCH
MCV
MDA
MDMA
MEAN CELL HEMOGLOBIN CONCENTRATION
Mebaral®
MECONIUM DRUG SCREEN
Medium chain acyl CoA dehydrogenase (MCAD)
Megaloblastic Anemia, Serum
MEK, Blood
Melanoma Monitor Profile
MENINGOCOCCUS GROUPS (A,B,C,Y,W135)
Meperidine (Demerol®), Serum
MERCURY
Mesoridazine (Serentil®), Serum
Metabolic Dysglycemia Profile
Mexate®
Mg, RBC
MGC GROUP B (SpinalFI)
MHA-TP
MIA Test
MIBK, Blood
MIC
Midstream Urine Culture, Routine
MILTOWN
MINIMUM BACTERICIDAL CONCENTRATION

APPENDIX

Miscellaneous Fluid Cytology
Mitochondrial Ab
MMAC
MMR
Mn, Blood
MNBK, Blood
MODIFIED ACID FAST STAIN
Mold Culture
MONO SCREEN
Morphine
MOTRIN
MPO-ANCA
MRSA Culture
msAFP
MTB, PCR (With Culture)
MTD
MTX, Blood
Mucin Clot Test
Multiple Endocrine Neoplasia (MEN2A)
MUMPS
MURAMIDASE TEST
MUSCLE BIOPSY
Myasthenia Gravis Antibody
MYCO -M
Myelin Basic Protein (MBP), Cerebrospinal Fluid
Myidone®
MYOGLOBIN
MYSOLINE
Na
NA
N-ACETYLPROCAINAMIDE
NAPA
NARCOLEPSY ASSOCIATED ANTIGEN
Nasal Smear for Eosinophils
NATIVE DNA
Navane®
NBT
N-DESALKYLFLURAZEPAM
Nebcin®
Necropsy
Neisseria gonorrhoeae by DNA Probe
NEMBUTAL
Neopterin
NERVE BIOPSY
Neuroblastoma Monitor Profile
NEWBORN HEMOLYTIC DISEASE WORKUP
NF-1, Known Mutation
NGI SuperQuantTM
NH3
NH4

APPENDIX

Ni, Plasma
Nickel, Plasma
Niemann-Pick Disease, DNA Analysis
Nipple Discharge
NITROBLUE TETRAZOLIUM, CGD
NKH1A, Leu19 (for CD56)
N-Methylacetamide
NMP 22
Nongonococcal Urethritis Culture
Noradrenaline, Plasma
Nose Culture
NSE
N-Telopeptide
NTX Test
Nuclear Matrix Protein (NMP) 22
O AND P
O2CT
OB HOLD REQUEST
OCCULT BLOOD
Ocular Cytology
OD 450
OGTT
OKT3 (CD3)
Oligoclonal Banding
ON SERVICES/ BLOOD BANK
ONE HOUR GDM
Opiate Confirmation, Urine
ORAL CYTOLOGY
Orbinamon®
Organism Identification
Ornithine transcarbamylase deficiency (linkage assay)
Oropharyngeal Brushings Cytology
Osmol
Ostase®
OVA AND PARASITE
OXALATE URINE
Oxidative Stress Analysis
OXYCODONE
P
P AND P TEST
P. carinii Pneumonia, Stain
p24 Antigen
PABA
Packed Cell Volume
PAIGG, PAIGA, PAIGM
Pamelor®
P-ANCA-Specific Antibody
Pancreatic Cancer Monitor Profile
PAP
PARA 3 AG DFA

APPENDIX

PAS
Paternity Studies
Pb, Blood
PBG DEAMINASE, ERYTHROCYTE
PCB Exposure Profile, Plasma
PCO2
PCP
PCR - CMV (SpinalFl)
PCV
PEDIGREE RECONSTRUCTION
PENTAZOCINE
PEPSINOGEN
PG and Creatinine, Amniotic Fluid
PG, Amniotic Fluid
PH
pH, Body Fluid
Phagocytosis
PHENAZOPYRIDINE
Philadelphia Chromosome
Phos
PHYTANATE
Pi Phenotype
Pill Analysis
Pinworm Preparation
Pituitary Glycoproteins, Alpha Subunit
PKU
PLACENTA EXAMINATION
PLEURAL FLUID
PLP
PLT
PNEUMO LATEX AGGLUTINATION
PO2
PO4
POLIO 1 ANTIBODY
PORCINE FACTOR VIII INHIBITOR TITER
Postmortem Examination
POTASSIUM
PP Glucose, Two-Hour
PPH
PPLO Antibodies
PPP
PR3-ANCA
PRA
Prealbumin
PRIMIDONE
Proaccelerin
PRUSSIAN BLUE STAIN
pS2 Protein, Paraffin Block
PSA
PSEUDOCHOLINESTERASE

APPENDIX

PSITTACOSIS
PT
PTH Intact
PTT
Punch Biopsy
PURKINJE CELL CYTOPLASMIC AB TYPE 1
PUS CULTURE
PYRALINKS-D
Q FEVER
QUAALUDE
Quick-Cult®
RA Latex
Random Blood Glucose
Rapid Grower Susceptibility Testing
Rash Profile A
RBC Cholinesterase
Recombinant Immunoblot Assay
Red Blood Cell (RBC) Antigen
Reference Bacterial Culture Identification
Rela®
Renal Function Panel
Replication Error
RER
Resistance Analysis
RET Mutations In MEN 2 And FMTC
Reverse T3
RF Assay
Rh Factor
Rheumatic Fever Profile
Rh-hr Genotype
Rho(D) Typing
RIBA HCV
Rickettsia rickettsii Titer
Ristocetin Cofactor
Ritalin®
RMSF IgM Antibodies
Rocket Fuel
Rotavirus, Direct Detection by Immunoassay
Routine Culture, Stool
RPR
RSV by DFA
Rubella Antibodies, IgG
S. pneumoniae Antigen
Saccharomonospora viridis
Salicylate, Serum
Sandimmune®
Sb, Urine
Scleroderma Diagnostic Profile
Scotch®
Se, Blood

APPENDIX

Secobarbital
Sedimentation Rate, Westergren
Selenium, Blood
Semen Analysis, Basic
Sensitivity Testing
Serentil®
Seven Drugs Plus Ethanol
SEX DETERMINATION
SGOT
SGPT
SHBG
Shingles Culture
Sickle Cell Anemia (Hb SS or SC)
Siderophilin
Silver, Plasma
Sinequan®
Sjögren's Antibodies (Anti-SS-A/Anti-SS-B)
Skeletal Alkaline Phosphatase (SALP)
Skin Biopsy ((To be assigned by pathologist))
SLE
SM-C/IGF-1
Smooth Muscle Antibodies
Snow
Sodium Fluoride
Soluble Transferrin Receptor
Soma®
Soprodol®
Soridol®
SPCA
Specific Esterase
Spinal and bulbar muscular atrophy (SBMA)
Spontaneous Abortion Chromosome Analysis
Sputum Culture
SRY/AZF Determination
ssay sensitivity)
St Louis Encephalitis Virus Antibodies, IgG
Stable Factor
Sterile Body Fluid Culture
sTfR
STH
Stimulation Test
Stool Culture
STR Analysis
STS
Stuart Factor
Styrene Exposure Profile
Sudan Black B
Sugar, Quantitative, Urine
Sulfate, Quantitative, 24-Hour Urine
SuperQuantTM HCV

APPENDIX

Surface Factor
Susceptibility Testing
Swamp Fever
Swineherd Disease
Synovial Fluid, Mucin Clot Test
Syphilis Serology
Systemic Lupus Erythematosus (SLE) Profile A
T- and B-Cell Gene Rearrangements
T Cell Receptor Beta Chain (TCRß)
T3
T3, Free
T4
T4, Free by Equilibrium Dialysis, Serum
T4/T8 Analysis
TAC Antigen
Tambocor®
Tape Test
Tartrate-Resistant Acid Phosphatase Stain
Tay-Sachs Disease, Biochemical, Leukocytes
TB Stat Test
TBG
TBili
TCA, Urine
T-Cell Activation Profile, CD8 Subsets
TCK
TCO2
TeBG
Tegretol®
Teichoic Acid Antibodies
Tempra®
Testicular Cancer Monitor Profile
Tetanus Antibodies
Thallium, Urine
THC
Theo-Dur®
Thiamine, Plasma
Thorazine®
Throat Culture
Thyrocalcitonin
TIBC
Tissue Karyotype
Titratable Acidity
Tl, Urine
TLI
T-Lymphocyte Helper/Suppressor Profile
TNF
Tobramycin (Nebcin®), Serum, Peak
Tofranil®
Toluene Exposure Profile
Topiramate (Topamax®), Serum

APPENDIX

Total Bili
Toxoplasma gondii Antibodies, IgG
TPO Antibodies
TProt
TRAb
Treponema pallidum Antibodies (FTA-ABS)
Triavil®
t-RNA Synthetase
Troponin I
True Cholinesterase
Trypsin
TSH Receptor Ab
TSI
Tularemia Agglutinins
Tumor Necrosis Factor-
Twin Zygosity, Pre- and Postnatal
Tylenol®
Type and Rh
Tyrosine Phosphatase Autoantibodies
Tzanck Smear
UA
UA, Routine
UIBC
UltraQualTM HCV
Unbound T3
Unconjugated DHEA
Undifferentiated Tumor Panel
Uniparental Disomy Profile
Unsaturated Iron Binding Capacity
Upper Respiratory Culture, Routine
Urea Clearance
Uric A
Uroporphyrin
Uterine Cancer Monitor Profile
UUN Clearance
Vaginal Cytology
Valium®
Vancocin®
Varicella-Zoster Virus (VZV) Antibodies, IgG
Vasoactive Intestinal Polypeptide (VIP), Plasma
VDRL, Cerebrospinal Fluid
VGCC Antibody
VIP
Viral Culture, General
Viscosity, Serum
Vitamin A and Carotene
VMA and Catecholamines
Volatiles, Blood
von Recklinghausen Disease
VRE, Culture Only

APPENDIX

vW Factor Assay
vWF Antigen
VZV by DFA
Warfarin (Coumadin®), Serum
WBC
WBlot HIV1
Weil Disease
Westergren Sedimentation Rate
Wet Prep
White Blood Cell (WBC) Count
Whole Blood Histamine
Wood Alcohol
Wound
Wright-Giemsa Stain
Wuchereria Smear
Xylenes Exposure Profile
Yeast Culture
Zarontin®
Zinc, Plasma/Serum
Zn, Serum
ZPP
ZYGOSITY TESTING

We claim:

1. A method for identifying a research subject, comprising:

- obtaining medical data from a subject;

- associating an identifier for said subject with said medical data in at least a first database;

- associating the identifier for said subject with the name and contact information of said subject;

- identifying criteria for selecting a research subject;

- extracting an identifier from the first database, wherein said identifier is associated with a subject matching the identified criteria; and

- matching the identifier from the first database with the name and contact information in order to identify the research subject.

2. The method according to claim 1, further comprising obtaining informed consent from said subject, wherein said informed consent permits the medical data to be used to identify said subject as a potential research subject.

3. The method according to claim 1, wherein medical data are obtained from said subject and associated with the identifier for said subject in at least a first database longitudinally.

4. The method according to claim 1, wherein said subject is a member of a group of donors, and said method is repeated for each member.

5. The method according to claim 1, wherein the subject is a deferred donor.

6. The method according to claim 1, wherein the medical data comprise a medical history.

7. The method according to claim 1, wherein the medical data comprise a family history.

8. The method according to claim 1, wherein the medical data comprise clinical chemistry test results.

9. The method according to claim 1, wherein the medical data comprise pharmacogenomic or genomic data.

10. The method according to claim 1, wherein the medical data comprise proteomic data.

11 The method according to claim 1, wherein the criteria include medical history information.

12. The method according to claim 1, wherein the criteria include family history information.

13. The method according to claim 1, wherein the criteria include clinical chemistry test results.

14. The method according to claim 1, wherein the criteria include pharmacogenomic or genomic information.

15. The method according to claim 1, wherein the criteria include proteomic information.

16. The method according to claim 1, wherein said first database is a computerized database.

17. The method according to claim 1, wherein the name and contact information is stored in at least a second database.

18. The method according to claim 17, wherein said first database and said second database are computerized databases.

19. The method according to claim 18, wherein the first and second databases are stored on separate computers.

20. The method according to claim 19, wherein the computer storing the first database is connected through a network firewall with the computer storing the second database.

21. The method according to 1, wherein the first database is a computerized database and is accessible through a network.

22. The method according to claim 21, wherein the network is a local area network or an intranet.

23. The method according to claim 21, wherein the network is an internet.

24. A method for identifying a research subject in a group of donors from at least one collection establishment, comprising:

a. obtaining a biological sample and medical data from a donor;

b. associating an identifier for said donor with said biological sample and medical data in at least a first database;

c. associating the identifier for said blood donor with the name and contact information of said donor;

d. identifying criteria for selecting a research subject;

e. extracting an identifier from the first database, wherein said identifier is associated with a donor matching the identified criteria; and

f. matching the identifier from the first database with the name and contact information in order to identify a research subject.

25. The method according to claim 24, further comprising obtaining informed consent from said blood donor, wherein said informed consent

permits the medical data to be used to identify said blood donor as a potential research subject.

26. The method according to claim 24, wherein medical data are obtained from said donor and associated with the identifier for said donor in at least a first database longitudinally.

27. The method according to claim 24, wherein said donor is a deferred donor.

28. The method according to claim 24, wherein the medical data comprise a medical history.

29. The method according to claim 24, wherein the medical data comprise a family history.

30. The method according to claim 24, wherein the medical data comprise clinical chemistry test results.

31. The method according to claim 24, wherein the medical data comprise pharmacogenomic or genomic data.

32. The method according to claim 24, wherein the medical data comprise proteomic data.

33. The method according to claim 24, wherein the criteria include medical history information.

34. The method according to claim 24, wherein the criteria include family history information.

35. The method according to claim 24, wherein the criteria include clinical test results.

36. The method according to claim 24, wherein the criteria include pharmacogenomic or genomic information.

37. The method according to claim 24, wherein the criteria include proteomic information.

38. The method according to claim 24, wherein said first database is a computerized database.

39. The method according to claim 24, wherein the name and contact information of said blood donor is stored in at least a second database.

40. The method according to claim 39, wherein said first database and said second database are computerized databases.

41. The method according to claim 40, wherein said first and second databases are stored on separate computers.

42. The method according to claim 41, wherein the computer storing the first database is connected through a network firewall with the computer storing the second database.

43. The method according to 24, wherein the first database is a computerized database and is accessible through a network.

44. The method according to claim 43, wherein the network is a local area network or an intranet.

45. The method according to claim 43, wherein the network is an internet.

46. A plurality of biological samples collected from at least one subject, wherein each sample is associated with an identifier linking said biological sample to at least one of medical data, genomic data, pharmacogenomic data, and proteomic data in at least a first database and wherein said biological samples are collected and stored longitudinally.

47. The plurality of biological samples according to claim 46, wherein said samples are whole blood, plasma, serum, blood cells, and proteins or nucleic acids isolated therefrom.

48. A plurality of biological samples collected from at least one donor, wherein each sample is collected at a collection establishment and associated with an identifier linking said donor and said biological sample to at least one of medical data, genomic data, pharmacogenomic data, and proteomic data in at least a first database and wherein said plurality of biological samples are collected and stored longitudinally.

49. A method for creating a database, the method comprising:

a. collecting a biological sample from at least one subject;

b. collecting a medical data from said at least one subject;

c. deriving proteomic information and genomic information from the sample;

d. storing the sample in a location from which the sample can be recovered;

e. associating the medical data, the proteomic information, and the genomic information with an identifier that can be used to locate the sample; and

f. performing steps a to e on the same subject longitudinally;

and wherein steps b to d may be performed in any order.

50. The method according to claim 49, wherein steps a to f are performed on multiple subjects.

51. The method according to claim 49, wherein the biological sample is whole blood, plasma, serum, blood cells, or proteins or nucleic acids isolated therefrom.

52. The method according to claim 49, wherein the samples are collected from at least one collection establishment.

53. The method according to claim 49, wherein said medical data comprises clinical chemistry test information.

54. The method according to claim 53, wherein the clinical chemistry test is at least one test selected from ABO/RH type, antibody screening tests, alanine aminotransferase (ALT) tests, cytomegalovirus (CMV) screening, hepatitis B screening, hepatitis B core antibody screening, hepatitis C screening, human immunodeficiency virus (HIV) types 1 and 2 screening, human T-cell lymphotropic virus (HTLV)-1 screening, and HIV antigen screening.

55. The method according to claim 49, wherein the genomic information includes DNA polymorphisms.

56. The method according to claim 49, wherein the DNA polymorphisms are single nucleotide polymorphisms.

57. The method according to claim 49, wherein the proteomic information includes the proteins expressed in the sample.

58. The method according to claim 49, wherein the genomic information includes the ribonucleic acids expressed in the sample.

59. The method according to claim 49, wherein said medical data comprises family histories from the subjects.

60. The method according to claim 49, wherein said medical data comprises demographic information from the subjects.

61. The method according to claim 49, wherein at least one of the medical data, the genomic information, the proteomic information, and the location for the sample is associated with an identifier for the subject that can be used to retrieve the name and contact information of said subject

62. A method for identifying a genomic or a proteomic characteristic which correlates with a disease, said method comprising:

- creating a database according to claim 48;
- identifying subjects with the disease;
- identifying genomic and proteomic characteristics shared by said subjects.

63. The method according to claim 62, wherein the genomic characteristic identified is a single nucleotide polymorphism.

64. The method according to claim 62, wherein the genomic characteristic identified is pharmacogenomic information.

65. The method according to claim 62, wherein the proteomic information is a change in protein level.

66. A method for recruiting a research subject for a clinical study, said method comprising:

- identifying said research subject according to claim 1 according to selected criteria; and

- contacting said research subject for recruiting said research subject for said clinical study.

67. A method for recruiting a research subject for a clinical study, said method comprising:

- identifying said research subject according to claim 24 according to selected criteria; and

- contacting said research subject for recruiting said research subject for said clinical study.

68. The method according to claim 27, wherein said deferred donor is a deferred blood or plasma donor.

Figure 1

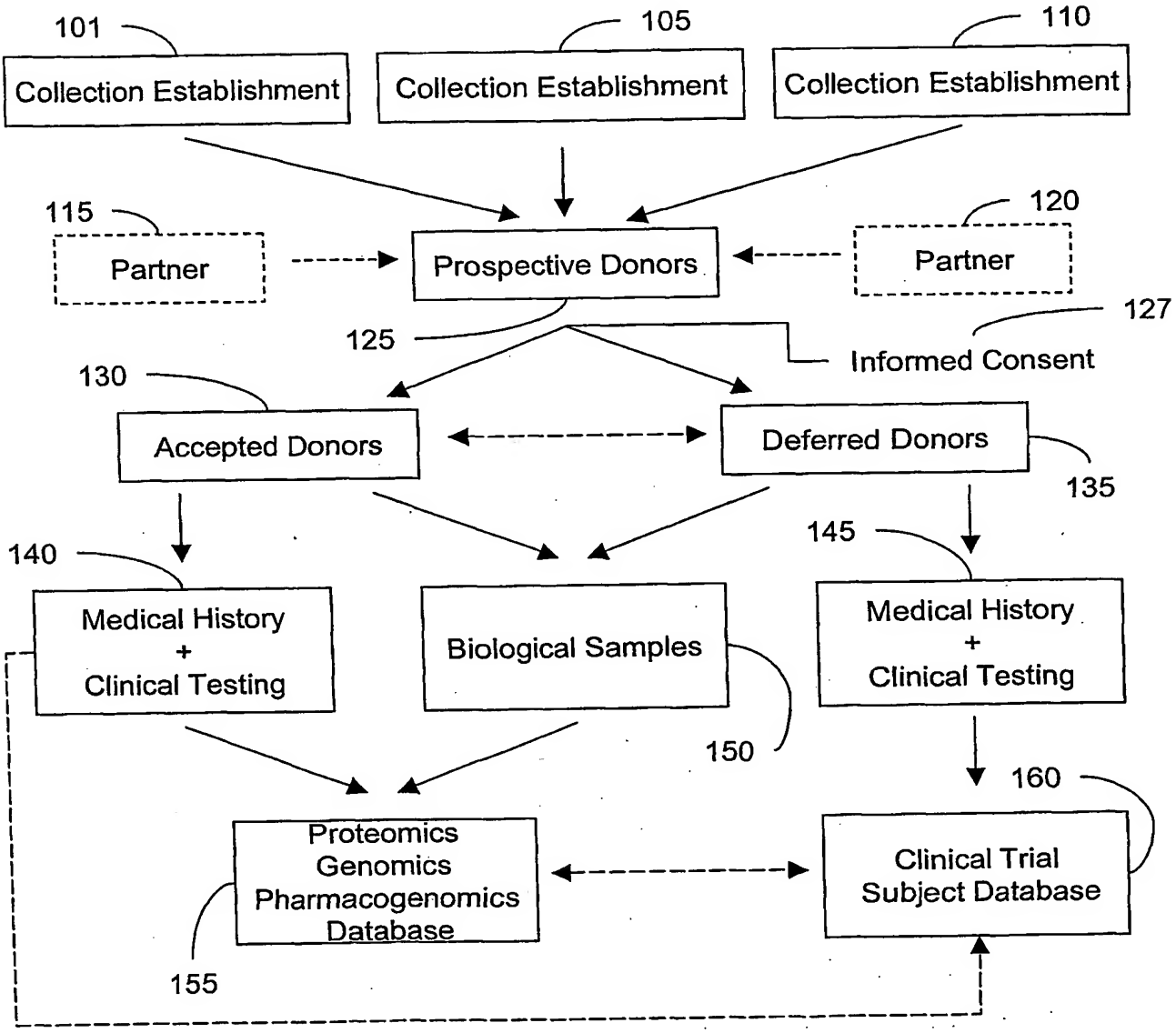

101
Collection Establishment
105
Collection Establishment
110
Collection Establishment
115
Partner
Prospective Donors
120
Partner
125
127
Informed Consent
130
Accepted Donors
Deferred Donors
135
140
Medical History
+
Clinical Testing
Biological Samples
145
Medical History
+
Clinical Testing
150
160
Proteomics
Genomics
Pharmacogenomics
Database
Clinical Trial
Subject Database
155

Figure 2

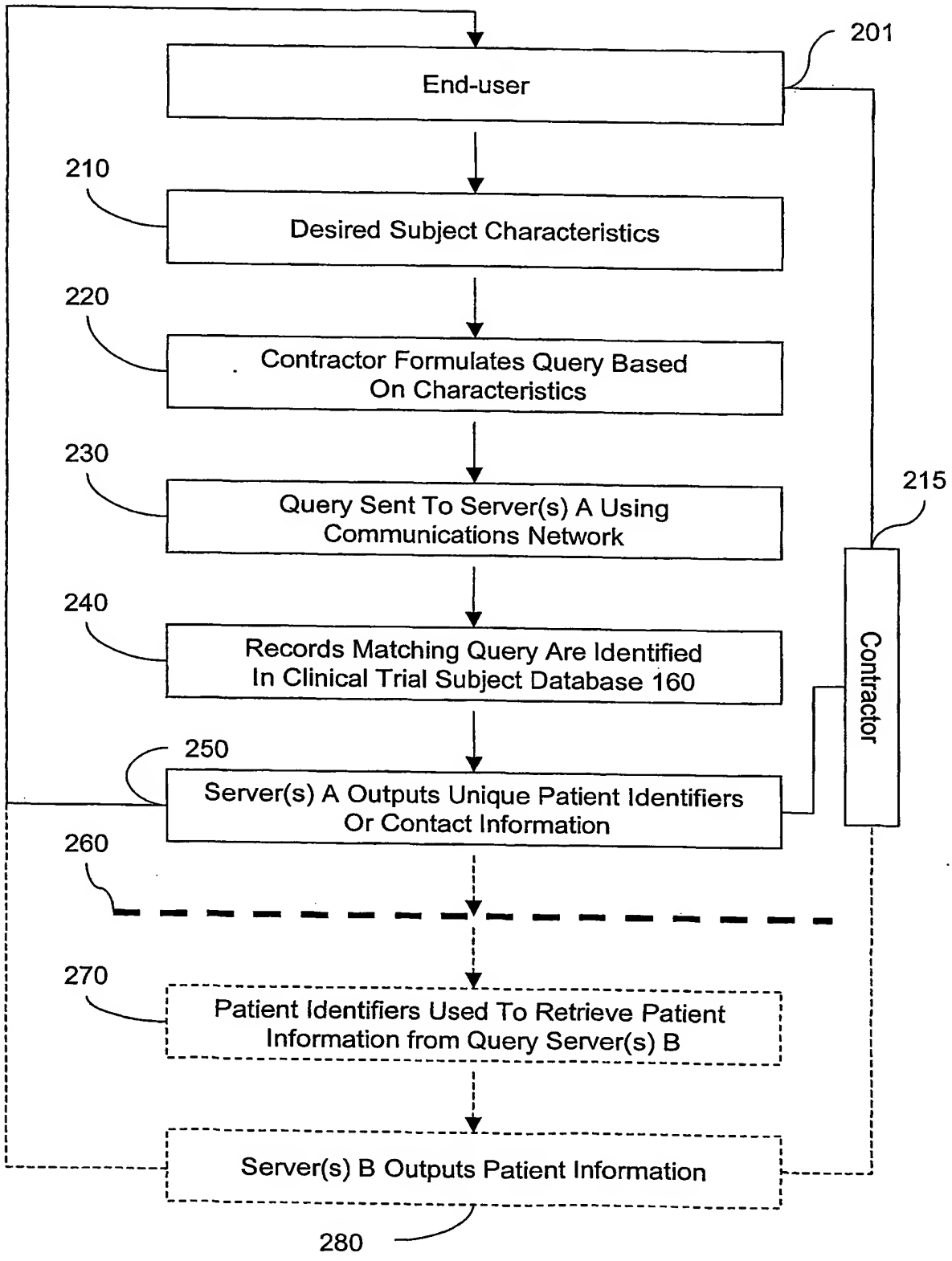

201
End-user
210
Desired Subject Characteristics
220
Contractor Formulates Query Based On Characteristics
230
Query Sent To Server(s) A Using Communications Network
215
240
Records Matching Query Are Identified In Clinical Trial Subject Database 160
Contractor
250
Server(s) A Outputs Unique Patient Identifiers Or Contact Information
260
270
Patient Identifiers Used To Retrieve Patient Information from Query Server(s) B
Server(s) B Outputs Patient Information
280

Figure 3

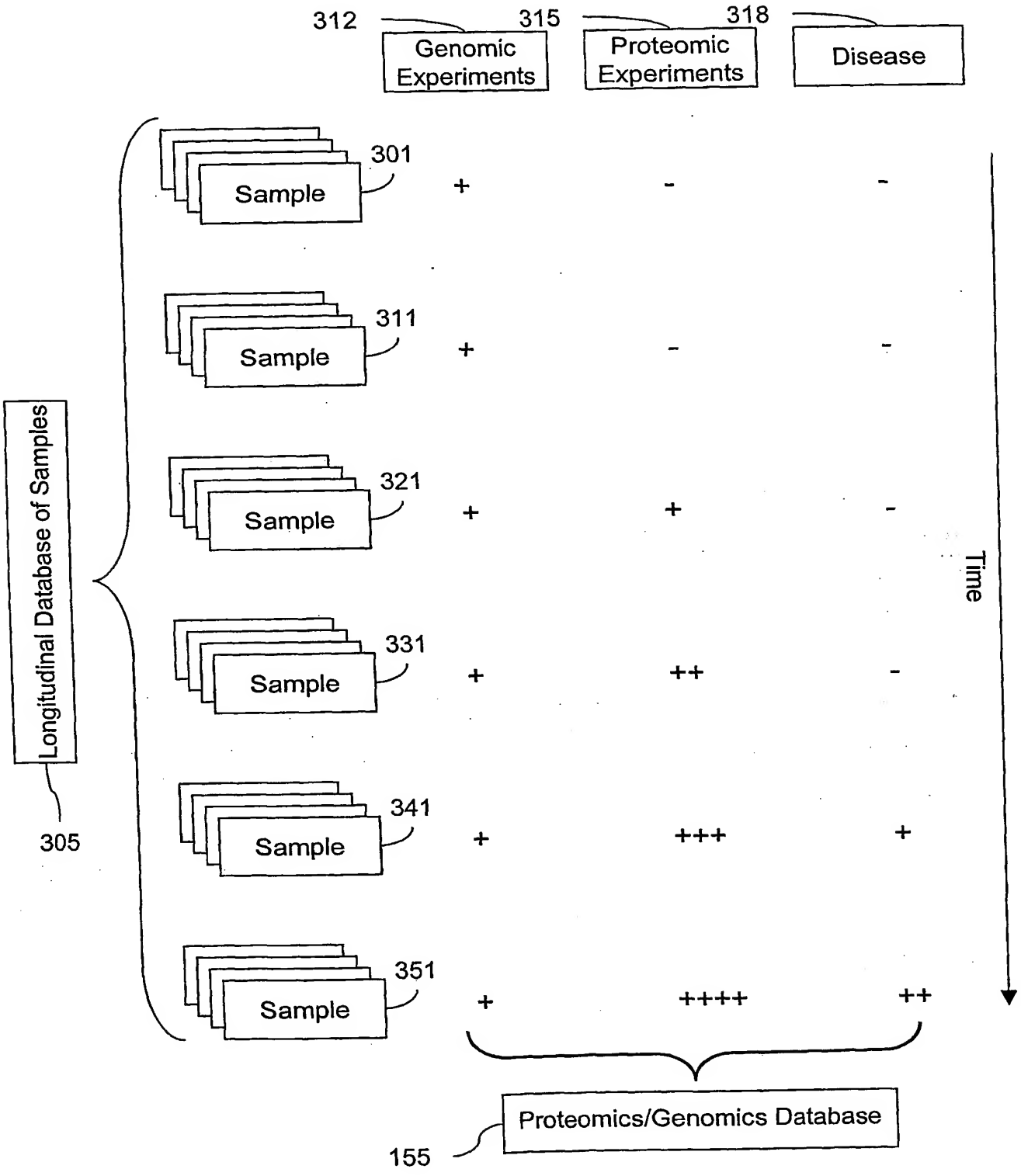


Figure 4

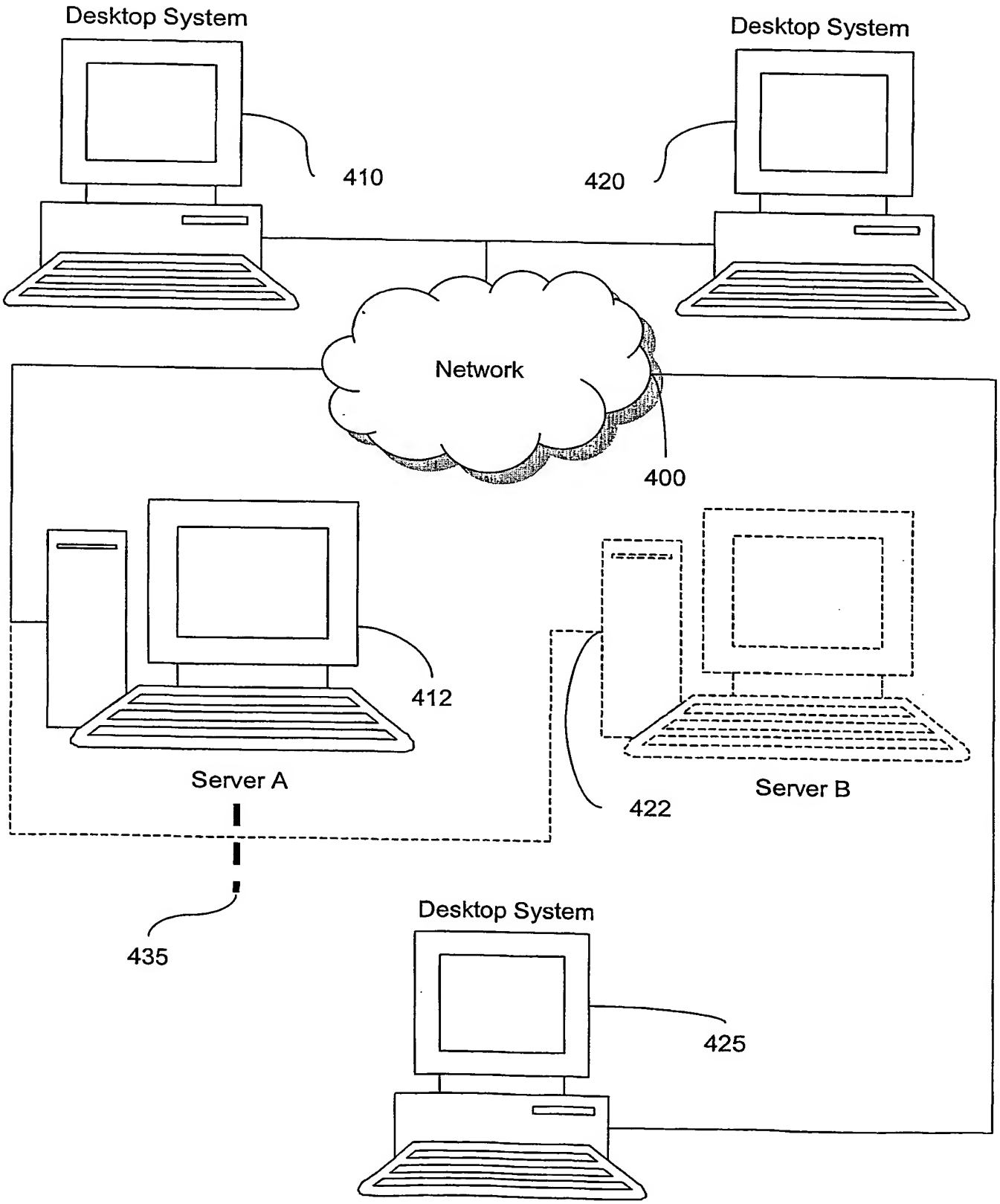
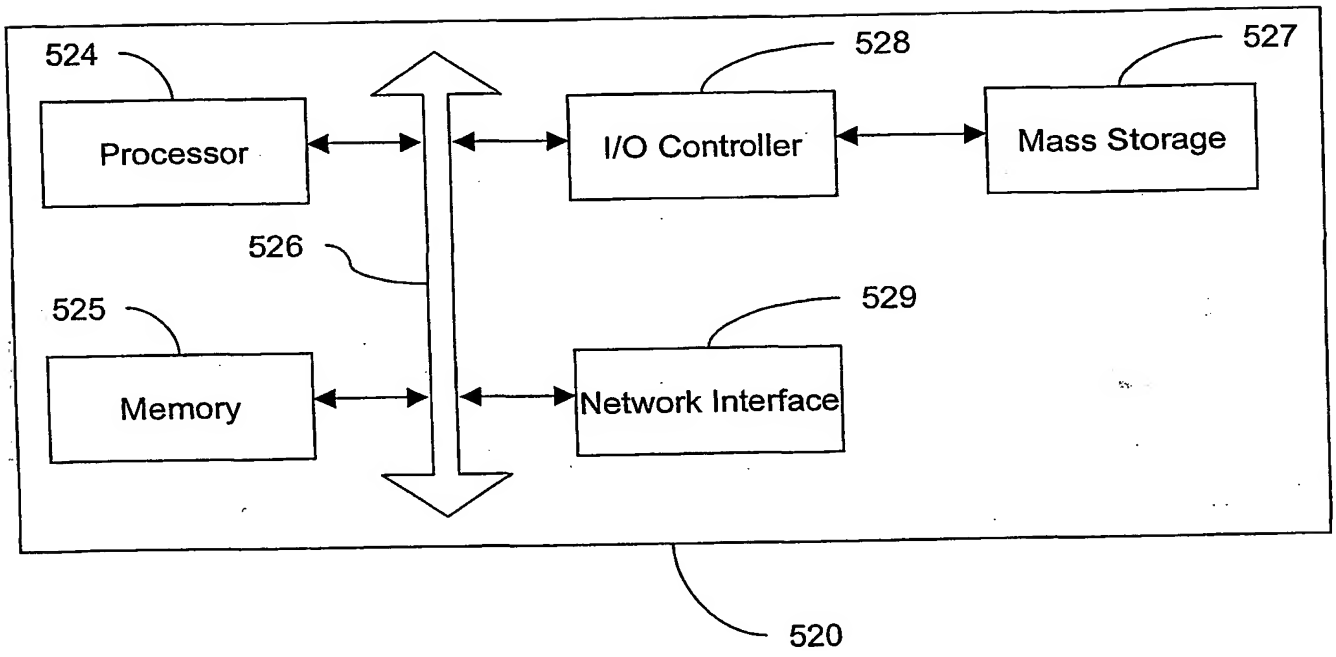


Figure 5



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 March 2002 (07.03.2002)

PCT

(10) International Publication Number
WO 02/17770 A3

(51) International Patent Classification[7]: A61M 1/00

(21) International Application Number: PCT/US01/26593

(22) International Filing Date: 27 August 2001 (27.08.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/227,910 28 August 2000 (28.08.2000) US

(71) Applicants and
(72) Inventors: **MORAND, Patrick, G.** [US/US]; 2529 Kingston Drive, Northbrook, IL 60062 (US). **OSTRO, Marc, J.** [US/US]; 23 West Shore Drive, Pennington, NJ 08534 (US).

(74) Agents: **GARRETT, Arthur, S.** et al.; Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., 1300 I Street, N.W., Washington, DC 20005-3315 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

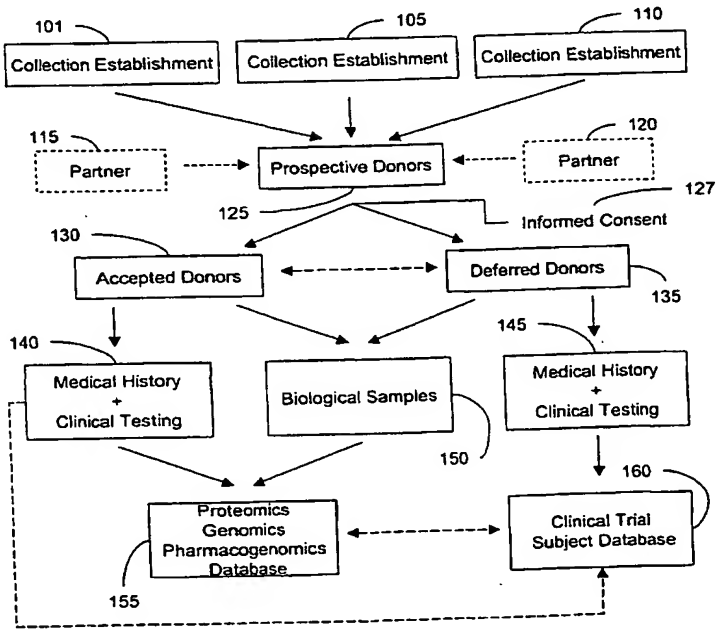
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
13 June 2002

[Continued on next page]

(54) Title: USE OF BLOOD AND PLASMA DONOR SAMPLES AND DATA IN THE DRUG DISCOVERY PROCESS



(57) Abstract: Systems consistent with the present invention provide a method for identifying and recruiting donors whose demographic characteristics, genomic and proteomic profile, and medical histories make them attractive candidates for clinical trials, drug target identification, and pharmacogenomic studies.

WO 02/17770 A3

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/26593

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61M 1/00
US CL : 604/30,31,66, 67

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/30,31,66, 67

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN on line

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,558,638 A (EVERS et al.) 24 September 1996, entire document.	1-45,49-61, 66-68
Y	US 5,970,499 A (SMITH et al.) 19 October 1999, claims 1-74.	1-45,49-61, 66-68
Y	US 5,809,493 A (AHAMED et al.) 15 September 1998, claims 1-20.	1-45,49-61, 66-68

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 14 JANUARY 2002	Date of mailing of the international search report 18 MAR 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Jayce Bridgers for MICHAEL BORIN Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/26593

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-45,49-61,66-68

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/26593

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional examination fees must be paid.

Group I, claims 1-45, 49-61, 66-68 drawn to method of identifying a research subject.
Group II, claims 46-48, drawn to a set of biological samples.
Group III, claims 62-65, drawn to method of identifying correlation of a disease with genomic or proteomic information.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art.
The method of Group I does not require the particular set of samples of Group II, Group I (as in claim 24) does not require plurality of samples, as required in claim 46, and there is nothing in the claims that identifies the particular set of samples of claim 46 as a special technical feature. Further, the latter set of samples would not be considered as a "special technical feature" as such samples are routinely obtained from any patient. Similarly, Group III utilizes database created using samples of Group II (note that Group II is drawn to samples rather than to a particular database created on the basis of these samples; the latter set of samples would not be considered as a "special technical feature" as such samples are routinely obtained from any patient).

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species for each group are as follows:

A) medical data comprise medical /family history or clinical chemistry;
B) medical data comprise genomic data;
C) medical data comprise proteomic data